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**14. ABSTRACT:** Prostate cancer is the most common cancer among men in the United States (IARC, 1995) and the second most common in the European Community (IARC, 1995). The causes of prostate cancer, however, remain largely unknown, with age, race, and family history being the only established risk factors (Nomura et al., 1997). The prostate gland has historically been considered the prototype of an androgen-dependent organ. However, there is evidence that estrogens may induce mitosis of prostatic epithelial cells in many species, including humans (Leav et al., 1978; Schulze et al., 1987). This report analyzes the association between prostate cancer and estrogen metabolism investigated in a case-control study. In particular, we tested the hypothesis that the pathway favoring 2-hydroxylation over 16α-hydroxylation may be associated with a decrease in prostate cancer risk. This is the annual report for the third year of the study. During the third year of activity, we completed the definition of the large dataset of the study, conducted quality control procedures on the collected data and develop new laboratory procedures for the determination of the estrogen metabolites using gas-chromatography. The determinations are in now in advanced phase of progress.

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## INTRODUCTION

Prostate cancer is the most common cancer among men in the United States (IARC, 1995) and the second most common in the European Community (IARC, 1995). The causes of prostate cancer, however, remain largely unknown, with age, race, and family history being the only established risk factors (Nomura et al., 1997). The prostate gland has historically been considered the prototype of an androgen-dependent organ. However, there is evidence that estrogens may induce mitosis of prostatic epithelial cells in many species, including humans (Leav et al., 1978; Schulze et al., 1987).

This report analyzes the association between prostate cancer and estrogen metabolism investigated in a case-control study. In particular, we tested the hypothesis that the pathway favoring 2-hydroxylation over 16α-hydroxylation may be associated with a decrease in prostate cancer risk.

This is the annual report for the third year of the study. During the third year of activity, we completed the definition of the large dataset of the study, conducted quality control procedures on the collected data and develop new laboratory procedures for the determination of the estrogen metabolites using gas-chromatography. The determinations are in now in advanced phase of progress.

## BODY OF REPORT

In accordance with the Statement of Work, during the third budget year, we are conducting hormone determinations as part of the planned activity are preparing the database for data analysis.

### Background

**Follow-up of the cohort**: We completed the re-call and follow-up of the Western-New York cohort (WNYHC) for the identification of the incident prostate cancer cases and their related control subjects. The follow-up was conducted in collaboration with another NIH-funded study, the "Epidemiology of Type-2 Diabetes" study, which is a prospective cohort study based on the same WNYHC cohort (RO1 DK 60587, Dr. R. Donahue, PI, Dr. P. Muti, Co-PI).

The re-call of the cohort started in January 2003. The re-call included participants without history of cancer, cardiovascular diseases, and clinically defined type-2 diabetes at baseline interviewed between 1996-2001. The re-call was also limited to those cohort participants with stored biological samples. Thus, we started the re-call and the follow-up process with a sample of **1,150 cohort participants**.

Of the 1,150 cases :-

- **52** were not eligible for medical reasons (too ill with diseases other than those mentioned before),
- **46** had died (for causes other than prostate cancer),
- **22** had moved out of the Erie and Niagara Counties,
- **117** were not contactable by mail or phone**.**

Overall, we had a sample of **913** re-called participants. Among the **913** participants, we identified :-

- **41** incident prostate cancer cases,
- **232** cases refused to participate in the study (they refer, in the short telephone interview, to having not been diagnosed with prostate cancer),
- **40** were scheduled but then cancelled the appointment,
- **8** were still in-process at the end of the follow-up period (September 30, 2004).

Thus, there were **592** participants available as control subjects.

During the study period, we monitored the occurrence of prostate cancer among the successfully contacted participants. All procedures to re-call, interview and collect biological specimens from the WNYHC Study were similar to the procedures used for baseline recruitment. All eligible participants were initially re-contacted by letter and then by phone (up to twelve callbacks). Participants were invited to attend our recruitment center at the Department of Social and Preventive Medicine, Buffalo, New

York for the clinical examination and to answer questions related to the occurrence of prostate cancer diagnosis between the baseline examination and the re-call time.

**Definition of the matched case-control pairs**.

Case Identification: Incident Prostate Cancer Cases: Prostate cancer cases recruited in the study were men who have been diagnosed with incident cytologically and/or histologically confirmed prostate cancer after their recruitment (date at first interview) in the WNYHC Study and before the end of the cohort follow-up period (September, 30, 2004). Prostate cancer cases were identified by their own report at the re-call of the cohort. 32 cases have been validated by their clinical records, while the remaining 9 cases are in the process to be validated. At recruitment, each cohort member signed a consent form giving us permission to request copies of their clinical charts in cases of pathological events related to the WNYHC Study investigations. Through these clinical charts, we are validating the information collected from participants.

Control Identification: Eligible controls were all male members of the WNYHC Study who, based on their report, were not diagnosed with prostate cancer at the diagnosis of the related case. For each prostate cancer case, four controls will be randomly chosen after matching for:

a) age (within 3 years);
b) race;
c) recruitment date

to control for the effect of long-term preservation of stored urine.

To increase the power of the study (and to reduce the effects of non-diagnosed prostate cancer cases among controls), we used a 1:4 ratio for cases and controls. Therefore, the study hormone determinations will be conducted on 41 prostate cancer cases and 164 control subjects.

At present, we have conducted a series of quality control procedures for laboratory determination of the estrogen metabolites included in the study. From these procedures, we have identified gas-chromatography as the most reliable method to assay these biomarkers. The actual determinations are on-going.

## KEY RESEARCH ACCOMPLISHMENTS

- Completed the follow-up of the cohort
- Completed quality control procedures to ensure the completeness (reliability?) of the follow-up
- Completed quality control setting for hormone bio-assays
- Completed new analysis of secondary sexual characteristics and prostate cancer risk, based on a previously DOD-funded prostate cancer study

## REPORTABLE OUTCOMES

Publications and Presentations

At this time, there are no results or publications coming directly from this grant because we still completing the study. However, Dr. Muti has published, or has in press, research on hormone-related cancer using a previously collected data set on hormone and prostate cancer (the dataset was originated from a previously DOD-funded study). She has submitted a paper for publication on the relationship between Indicators of Sexual and Somatic Development and Adolescent Body Size in Relation to Prostate Cancer Risk: Results from a case-control study.

In 2005-2006, Dr. Muti has published other papers on hormones and cancer, listed below:

1) Barba M, McCann S, **Muti P**, Stranges S, Fuhrmann B, Trevisan M, Freudenheim JL Perinatal *Exposures and Breast Cancer Risk: a Case Control Study (in press,* Cancer Causes and Control)

2) Colombo C, **Muti P**, Pala V, Cavalleri A, Venturelli E, Locardi M, Berrino F, Secreto G*. Plant-based diet, serum fatty acid profile, and free radicals in postmenopausal women: the diet and androgens (DIANA) randomized trial*. Int J Biol Markers. 2005 Jul-Sep;20(3):169-76

3) McCann se, Kulkarni S, Trevisan M, Vito D, Nie J, Edge S, **Muti P**, Freudenheim JL *Dietary lignan intakes and risk of breast cancer by tumor estrogen receptor status (in press*, Breast Cancer Research and Treatment)

4) *Cavalieri E, Chakravarti D, Guttenplan J, **Muti P**, Jankowiak R, Rogan E, Russo J, Santen R, Sutter T* Catechol Estrogen Quinones as Initiators of Breast and Other Human Cancers. Implications for Cancer Prevention and Biomarkers of Susceptibility (submitted for publication)

She has also presented new study results from other studies conducted, at the Meetings of the American Association for Cancer Research:

1) **Teter B***, Cavalleri A, Fuhrman B, Krogh V, Barba M, Schünemann HJ, Evangelista A, Del Sette D, Micheli A, Meneghini E, Secreto G, Berrino F, **Muti P** *Urinary Nocturnal Excretion of 6-sulfatoxymelatonin and Breast Cancer Risk* Meeting of the American Association for Cancer Research "Frontiers in Cancer Prevention Research", Baltimore, October 2005

2) **Barba M***, Cavalleri A, Schünemann HJ, Krogh V, Evangelista A, Secreto G, Micheli A, Qi Zhou, Fuhrman B, Reter B, Berrino F, Muti P *Effects of different storage temperatures on 6-Sulfatoxymelatonin concentration in urin* Meeting of the American Association for Cancer Research "Frontiers in Cancer Prevention Research", Baltimore, October 2005

3) Crespo CJ, **Fuhrman B***, Smit E, Freudenheim JL, Garcia Palmieri M, Lee IM, Muti P, Marrero FR. *Anthropometric Measures and Fasting Glucose as Predictors of Fatal Prostate Cancer among Puerto Rican Men: The Puerto Rico Heart Health Study Cohort* Meeting of the American Association for Cancer Research "Frontiers in Cancer Prevention Research", Baltimore, October 2005

4) Barba Maddalena, **Terrenato Irene**, Fuhrman Barbara, Teter Barbara, Schunemann Holger, Muti P. *Secondary sexual characteristics and body size at different ages in relation to risk of prostate cancer: results from a case-control study* Annual Meeting American Association for Cancer Research,Washington, April 2006

Two of these studies have been submitted for publication.

In addition, Dr. Muti has several other manuscript submitted for publication on hormone and related factors and cancer.

## CONCLUSIONS

The phase of hormone determinations for this grant is on-going. Therefore, there are no conclusions to report at this time.

## REFERENCES


1) Barba M, McCann S, **Muti P**, Stranges S, Fuhrmann B, Trevisan M, Freudenheim JL *Perinatal Exposures and Breast Cancer Risk: a Case Control Study (in press,* Cancer Causes and Control*)*

2) Colombo C, **Muti P**, Pala V, Cavalleri A, Venturelli E, Locardi M, Berrino F, Secreto G*. Plant-based diet, serum fatty acid profile, and free radicals in postmenopausal women: the diet and androgens (DIANA) randomized trial*. Int J Biol Markers. 2005 Jul-Sep;20(3):169-76

3) McCann se, Kulkarni S, Trevisan M, Vito D, Nie J, Edge S, **Muti P**, Freudenheim JL *Dietary lignan intakes and risk of breast cancer by tumor estrogen receptor status* (*in press,* Breast Cancer Research and Treatment)

## APPENDIX

1) **Appendix 1:** Barba M, Terrenato I, Schünemann HJ, Fuhrman B, Teter B, Gallucci M, D'Amato A, **Muti P**. *Secondary sexual characteristics and adolescent body size in relation to risk of prostate cancer: results from a case control study (submitted for publication)*

# Secondary sexual characteristics and adolescent body size in relation to risk of prostate cancer: results from a case-control study.

Barba Maddalena[1], Terrenato Irene[1], Schünemann Holger J. [1,2,3], Fuhrman Barbara[4], Teter Barbara[4], Gallucci Michele[5] , Muti Paola[1,6]

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**Abstract**

BACKGROUND: Prostate cancer is currently the most frequently diagnosed cancer and the second leading cause of cancer death among men in the United States. Although it is a disease of older age, early physical growth and development might be important determinants of prostate cancer risk during adult life. Early onset of secondary sexual characteristics and adolescent anthropometrical characteristics have been investigated in relation to prostate cancer risk with inconsistent results.

*OBJECTIVE:* The purpose of this study was to examine the relationship between age at first shaving of facial hear, age at maximum shoe size and body size at age 10-13, considered as indicators of sexual and somatic development and surrogates of exposure to sex steroid hormones, and risk of prostate cancer.

*METHODS:* We conducted a population-based case-control study in Erie and Niagara counties, New York, USA. Cases included 64 men, aged 49-83 years, diagnosed with incident, primary, histologically confirmed and clinically apparent (stage B and higher) prostate cancer. Controls included 218 men, frequency matched on age and residential area. Information regarding the variables of interest were self-reported. We compared adjusted means of age at first shaving and age at maximum shoe size and calculated the odds of body size at age 10-13 using logistic regression models.

*RESULTS:* Cases and controls did not statistically differ with regard to age at first shave (18.0 vs. 17.8, $p = 0.46$), but they differed significantly for age at maximum shoe size (20.1 vs. 17.6, $p < 0.05$). In referral to body size at age 10-13, participants who defined themselves as heavy and heavier than peers had a decreased prostate cancer risk

when compared to participants who defined themselves thinner than peers (OR: 0.36 95% CI: 0.15-0.83 and OR: 0.38 95% CI 0.17-0.87, respectively).

*CONCLUSIONS:* Based on our study results, prostate cancer risk was statistically related to age at maximum shoe size and body size at age 10-13, but not to age at first shaving. Our findings underline the relevance of exposure to sex steroid hormones during critical windows of prostate gland development, evaluated throughout surrogates of hormonal milieu, in affecting prostate cancer risk later in adulthood.

## Introduction

Prostate cancer is the most frequently diagnosed malignancy and the second leading cause of cancer death among men in Western countries (1). Notwithstanding the importance of this malignancy, little is understood about its cause. Age, family history, race and country of residence are the only well established risk factors (2).

Over the last decades, the body of evidence regarding a major role of sex steroid hormones, particularly androgens, in prostate carcinogenesis has been considerably growing. A powerful tumor-promoting activity of androgens clearly emerges from animal data (3), while epidemiologic studies have produced conflicting results (4-8). Difficulties in identifying etiologically relevant time periods of exposure to sex steroid hormones through investigations conducted during adult life might partly explain inconsistency across epidemiologic studies.

It has been suggested that prostate sensitivity to hormonal influences widely varies over lifetime with particularly important influence during puberty, when this gland achieves its full development (9-10). At the same time, sex steroid hormones play a key role in

regulating sexual and somatic maturation in both genders, concurring to determine secondary sexual characteristics and measures of body size at different ages (11-12).

In this population-based case-control study we investigated the relationship between surrogates of hormonal milieu in adolescence and prostate cancer risk later in adulthood, focusing on self reported age at first shaving, age at maximum shoe size and body size at age 10-13.

## Materials and Methods

*Study Subjects*

We conducted a case-control study of incident, primary, histologically confirmed prostate cancer cases in Erie and Niagara counties, NY (the PROMEN study). We previously described the recruitment of study participants (13). In brief, from December 1998 to April 2001, 504 prostate cancer cases were identified. Of these 504, 163 met eligibility criteria, and were approved by the urologists and invited to join the PROMEN study. After being contacted, 50 men refused to participate. Thus, among the eligible participants, 70% (113/163) participated in the study. Twenty-five prostate cancer cases did not provide blood samples and 24 had missing data items, thus the present analyses are conducted on 64 cases.

To exclude latent prostate carcinomas that one cannot distinguish from those that would not progress to clinical disease (real latent carcinoma) and those detected in a very early phase of their progression, the present study included only patients with clinically apparent disease [stage B and greater by the staging system proposed by Catalona (14)].

To standardize the stage of the disease across hospitals, a screening form developed in the context of the PROMEN study was completed by a trained nurse case-finder using the hospital pathology records. The forms and hospital records were reviewed by the principal investigator (P. Muti) of the study.

In recruiting controls, since latent prostate carcinoma has a high prevalence in men over 50 (15), we evaluated serum prostate specific antigen (PSA). Those found to have a PSA level higher than 4 ng/ml were excluded from the control group, in accordance with the criterion adopted by the American College of Preventive Medicine (16), until the completion of further diagnostic procedures, that allowed us to clarify which of the two groups they truly belonged on the basis of their correct case-control status. We identified eight prostate cancer cases because of PSA determination in subjects who initially were recruited as controls.

Three hundred and seventeen of the 513 subjects contacted during the study period were willing to participate (61,8%). Participants with missing data for any of the variables of interest were excluded, thus the final sample includes 218 controls.

Information regarding age at first shave, age at maximum shoe size and body size at age 10-13 were self reported. With regard to body size at age 10-13, participants defined themselves thinner than, as heavy as or heavier than peers during the considered period.

Trained interviewers collected extensive data on demographics and other study variables during in person interviews. Waist circumference was measured by trained personnel using a standardized protocol. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters ($kg/m^2$).

All participants provided informed consent; the Human Subjects Review Board of the University at Buffalo, School of Medicine and Biomedical Science and each of the participating hospitals approved procedures for protection of human subjects in the study.

*Statistical Analysis*

Distributions for all variables of interest were examined. In order to evaluate the statistical significance of any associations between case/control status and participant characteristics, we used t-tests for continuous variables and Pearson's chi-square tests for categorical variables.

Adjusted means and standard errors for age at first shave and age at maximum shoe size (continuous variables) were obtained using a general linear model, while unconditional logistic regression was used to compute crude and adjusted odds ratios (OR) and 95% confidence interval (CI) for body size at age 10-13 (categorical variable). The same models were used to test variables for possible interactions (we considered significant an interaction with a p-value $< 0.05$) . In assessing risk estimates, age in years, race and BMI were considered as possible confounders. Each of the three outcome variables (age at first shaving, age at maximum shoe size and body size at age 10-13) was further mutually adjusted for the others. Subgroup analyses were also performed stratifying by race.

Given the different response rate between cases and controls, we compared the two groups on the basis of indicators of social-economic status and lifestyle factors available from our in-person interview (years of education, annual income, marital status, smoking status).

Furthermore, we examined the characteristics of men included in the present analyses (cases = 64 and controls = 218) and those of men who had been excluded because of missing data (cases = 24 and controls = 33 ) by case-case and control-control comparison.

Data were analyzed using SPSS version 11.5 (SPSS, Inc., Chicago, IL).

**Results**

Table 1 shows descriptive characteristics of study participants. When compared to controls, prostate cancer cases were more likely to be slightly younger, to have higher values of waist circumference and BMI and to be Afro-Americans. Non-significant associations were observed for history of enlarged prostate, familiar history of prostate cancer, and years of education.

In table 2, we report unadjusted and adjusted means for age at first shave and age at maximum shoe size, as well as crude and adjusted ORs and 95% CI for body size at age 10-13. When comparing mean values for age at first shaving and age at maximum shoe size, cases were likely to be older than controls (17.7 vs. 17.1, $p < 0.05$ and 19.7 vs. 17.9, $p < 0.05$, respectively). After adjustment for age, race and BMI, cases and controls did no longer statistically differ with regard to age at first shave (18.0 vs. 17.8, $p = 0.46$), while estimates resulted significantly different in terms of age at maximum shoe size (20.1 vs. 17.6, $p < 0.05$). With reference to body size at age 10-13, participants who defined themselves as heavy as peers and heavier than peers showed a decreased prostate cancer risk when compared to participants who defined themselves thinner than peers (OR: 0.36 95% CI: 0.15- 0.83 and OR: 0.38 95% CI 0.17- 0.87,

respectively). In computing risk estimates for each of the considered variables, neither mutual adjustment for the remaining two variables nor stratifying by race did significantly affect prostate cancer risk. Furthermore, no evidence for interaction was found in these data for any of the variables of interest.

When comparing cases and controls on the basis of indicators of social economic status and lifestyle factors, no significant differences emerged. Finally, from the comparative analysis by case-case and control-control comparison, participants who had been included in the present analyses differed from those who had been excluded because of missing data items exclusively for waist circumference ( $p < 0.05$ in both groups).

**Discussion**

On the basis of our case-control study results, prostate cancer risk was statistically related to age at maximum shoe size and body size at age 10-13, but not to age at first shaving. Our findings underline the relevance of exposure to sex steroid hormones during critical windows of prostate gland development in affecting prostate cancer risk later in adulthood.

Our study has several strengths. We had a population-based sample with clearer distinction between cases and controls than in previously conducted studies. This is the result of an innovative recruiting strategy, that is, limiting eligibility for enrolment as cases to men who have been diagnosed with advanced cancer stages (stage B and higher). This approach has been helpful in reducing misclassification by eliminating early stage prostate cancers, as they are not distinguishable from latent diseases that might be prevalent among controls. With the same aim, subjects were eligible for

recruitment as controls on the basis of a PSA determination, which helped to ensure that the control group was free from latent prostate cancer.

Additionally, in-person interviews conducted by trained personnel allowed the collection of a great variety of data on demographics, lifestyle, personal risk factors for prostate cancer (e.g. familial history) and three different surrogates of hormonal milieu relative to adolescence.

This study also has several limitations. A possible selection bias might have derived from a lower response rate among controls than among cases (61.8% vs. 69%). To address this issue, we compared cases and controls on the basis of several indicators of social-economic status and lifestyle factors available from our in-person interview. We found no evidence that controls were more health conscious or healthier than cases.

Another source of bias might have been introduced in our study by excluding study participants with missing data items for the variables of interest. Comparative analyses by case-case and control-control comparison showed significant differences exclusively for waist circumference, which did not represent outcome variables in the present study.

The reliance on self-reported age at first shave, age at maximum shoe size and body size at age 10-13 represents another possible study limitation. Independently on the study design, with adolescence being the exposure period under investigation, self-reporting represents the assessment methodology consistently used to collect information regarding the variables of interest across several studies conducted over the past two decades (17-20). Besides, scientific evidence shows a high degree of reproducibility of self-reported past body size measures in older persons (21).

Our study small sample size might have limited our ability in detecting significant differences for all the variables of interest. Nevertheless our findings add evidence to the potential role of preadult hormonal exposures in affecting prostate cancer risk later in adulthood, thus contributing to reduce a major gap currently existing in scientific knowledge of prostate carcinogenesis.

Although potentially of great meaning in clarifying aspects of prostate carcinogenesis, the relevant exposure period for the association between preadult hormonal influences and prostate cancer has been addressed in a few studies, extremely heterogeneous (17-20).

To our knowledge, the potential relationship between age at shaving initiation and prostate cancer risk has been exclusively investigated in a large, multiracial cohort study conducted by Habel and colleagues. Consistent with our study results, there was no overall association between age at shaving initiation and prostate cancer risk, although data lent some support for a week, non-significant association among non-white men who started shaving at a younger age (17).

The search of scientific literature with regard to previously conducted studies investigating the association of age at maximum shoe size with prostate cancer risk did not produce any result, making at the same time our study innovative and our finding not comparable.

Results from two recently conducted case-control studies did not provide any support to the association between past body size measures and prostate cancer risk (18-19). Differences in the study design (18), variables of interest and considered period of exposures (19), might partly explain the discrepancy with our results.

Consistent with our study, higher reported level of adiposity at age 10, evaluated by mean of pictograms representing figures ranging from thin to obese, resulted prospectively associated with a lower risk of prostate cancer from the analyses conducted by Giovannucci and colleagues using data from the Health Professionals Follow-up study (20).

Adolescence represents a critical window in prostate development, being this gland essentially dormant until its occurrence. Over this lifetime period, sex steroid hormones play a central role in the acquisition and maturation of an individual sexual and somatic characteristics, as well as in the achievement of prostate gland full development.

Furthermore, since sex steroid hormones are well documented regulators of prostate epithelial cell mitogenicy (22), the hormonal milieu associated with growth and development might influence the likehood of the occurrence and propagation of mutations at a cellular level.

At this regard, scientific literature is consistent in providing evidence of prostate cancer precursor lesions among men in their twenties, suggesting an early beginning of the carcinogenetic process and an important role of early life exposures (23).

Overweight and obesity in young males are associated with well documented endocrine aberrations, including higher estrogen and lower testosterone levels (24-25). This might provide some protection against prostate cancer, explaining, with regard to our study results, a lower risk among cases who reported a greater body size at age 10-13. Conversely, thinner young men are exposed to the same hormonal influences in an opposite balance.

In our study, cases showed a consistent delay in completing their sexual and somatic development, as expressed by an older age at shaving (although non significant in our limited sample) and at reaching maximum shoe size. This might suggest a lower sensitivity to testosterone, as a consequence of the exposure to higher circulating levels than in heavier participants. Further speculation about the underlying biological mechanisms would be only theoretical, being the scientific evidence very limited.

Conclusively, our need to reach a better knowledge about the preadult and, more specifically, the adolescent exposure to sex steroid hormones is undeniable and in deep contrast with the current lack of scientific evidence. Further work is needed in terms of specifically targeted studies, which are expected to be more homogeneous with regard to the study design, variables of interest and period of exposure, being these issues of crucial importance in the comparison and interpretation of the scientific results.

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**Table 1. Participants Descriptive Characteristics[1] by Case-Control Status (n=282).**

**PROMEN STUDY 1998-2001**

| | Cases (n = 64) | Controls (n = 218) |
|---|---|---|
| **Age (yr)** | 67.6 (7.9) | 70.1 (6.2)* |
| **Waist circumference (cm)** | 105.6 (13.6) | 101.8 (12.2)* |
| **BMI[2]** | 30.2 (5.1) | 28.5 (4.6)* |
| **Education (yr)** | 13.1 (2.9) | 13.0 (2.7) |
| **History of enlarged prostate** | | |
| % Yes | 56.2 | 44.0 |
| **Familial history of Pca** | | |
| % Yes | 15.6 | 10.1 |
| **African-American** | | |
| % Yes | 32.8 | 7.3*** |

[1] Values are means and standard deviations (SD), unless otherwise specified

[2] BMI calculated by Quetelet's index: weight(kg)/height ($m^2$)

*$p < 0.05$ **$p < 0.01$ ***$p < 0.001$

**Table 2. Prostate Cancer Risk Estimates. PROMEN STUDY, 1998-2001.**

| | | Unadjusted means and Standard Deviation | | Adjusted[1] Means and Standard Error | |
|---|---|---|---|---|---|
| **Age at first shave** | Cs | 17.7 (2.4) | | 18.0 (0.2) | |
| | Co | 17.1* (1.8) | | 17.8 (0.3) | |
| **Age at maximum shoe size** | Cs | 19.7 (9.4) | | 20.1 (0.7) | |
| | Co | 17.9* (3.5) | | 17.6* (0.7) | |
| **Body size at age 10-13** | **cs/co** | **Crude OR** | **95% CI** | **Adjusted OR** | **95% CI** |
| Thinner than peers | 18/27 | 1 | | 1 | |
| As heavy as peers | 22/104 | 0.32** | 0.15-0.67 | 0.36* | 0.15-0.83 |
| Heavier than peers | 24/87 | 0.41* | 0.20-0.87 | 0.38* | 0.17-0.87 |

[1] Adjusted for age, race and BMI
* p< 0.05 ** p<0.01